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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/086,206	02/28/2002	Juana Magdalena	408.014-CON	1829

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EXAMINER

JOHANNSEN, DIANA B

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 02/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/086,206

Applicant(s)

MAGDALENA ET AL.

Examiner

Diana B. Johannsen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 11 October 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 28-44 and 47-55 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 28-44, 47-51, 54 and 55 is/are rejected.
- 7) ☒ Claim(s) 52 and 53 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 09/242,588.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. This action is responsive to the complying complete set of claims filed 11 October 2005. Claims 28-30, 33-35, 37-40, 42, 44, 47-49, and 54-55 have been amended and claims 45-46 have been canceled. Claims 28-44 and 47-55 are now pending and under consideration. Any rejections not reiterated in this action have been withdrawn. **This action is NON-FINAL.**

#### ***Claim Objections***

2. Claims 52-53 remain objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

#### ***Claim Rejections - 35 USC § 112***

3. Claims 28-44, 47-51, and 54-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 28-44, 47-51, and 54-55 are indefinite over the recitation of the term "specific" in the claims, for reasons set forth in the prior Office action of 1 July 2004. The response argues that "one skilled in the art would readily understand that the term 'specific' is used to denote nucleic acid sequences that enable one to differentiate the members of *M. tuberculosis* complex from other bacteria, in particular, to differentiate BCG from other members of *M. tuberculosis* complex as indicated in lines 24 to 27 of page 4 and line 34 of page 4 through line 10 of page 5." This argument has been

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thoroughly considered but is not persuasive. Neither the specification nor the prior art provides a definition of this term that makes clear what the term means within the context of the invention, such that the manner in which the term "specific" limits either the structural and/or functional properties of the molecules of the claims would be clear to a skilled artisan. The discussion in the specification at pages 4-5 does not make clear what properties are required to meet the requirements of the claims.

Claims 31-32 remain indefinite over the recitation of the phrase "a nucleic acid sequence of claim 28" for the reasons set forth in the Office action of 1 July 2004. It remains unclear how this claim relates back to claim 28, as whether claims 31-32 in fact require the complete "nucleic acid" of claim 28. Clarification is required.

Claim 34 is indefinite because it is unclear how or whether the claim limits claim 33, from which it depends. Claim 33 is limited to a molecule that contains "a maximum of 21 base pairs," while claim 34 is drawn to a "nucleotide probe of claim 33 comprising 24 consecutive nucleotides....". Thus, it appears that claim 34 may not further limit claim 33, as is required of a proper dependent claim. Clarification is required.

Claims 42-44, 47-51, and 54-55 are indefinite over the recitation of the limitations "the nucleotide sequence of sequences adjacent to the senX3-regX3 region in the 3' of senX3 region," and "the nucleotide sequence of sequences adjacent to the senX3-regX3 region in the 5' of regX3 region" in claims 42, 47, 54, and 55. There is insufficient antecedent basis for the limitations "the nucleotide sequence...", "the senX3-regX3 region...", "the 3' of senX3 region," and the 5' of regX3 region" in the claims, as the claims do not previously refer to these sequences/regions. The claims should be

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amended so as to provide a clear and limiting structural and/or functional description of those primers that are intended to be encompassed by the claims.

Regarding claim 43, it remains unclear whether each primer of the pair of claim 42 must comprise 19 nucleotides, or whether this limitation applies only to one primer of the pair. Applicant is reminded that a proper dependent claim must further limit the claim from which it depends.

Claims 47-51 are indefinite because it is unclear whether the claims are drawn to a method for detection a strain "of M. tuberculosis complex," as set forth in the preamble of claim 47, or to a method for detection of M. tuberculosis, as set forth in the final process step. Clarification is required.

With further regard to claims 47-51, the relationship between steps 2-3 of claim 47 are unclear. It is noted that step 3 refers both to contacting the probe with "the biological sample" and with "amplified sequences." It is not clear whether step 3 is to be performed using sequences amplified in step 2, or using the original "biological sample." Clarification is required.

Claim 55 remains indefinite over the recitation of the limitations "the biological sample" and "the specific nucleic acids" in step (1), because there is insufficient antecedent basis for these limitations in the claim.

Claim 55 is indefinite because it is unclear as to whether the claim is drawn to a method "of detection and of differential diagnosis of BCG and the members of M. tuberculosis complex" as set forth in the preamble of the claim, or merely to a method for detecting the presence of non-BCG M. tuberculosis strains, as indicated in the final

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process step. Particularly, it is noted that the claim does not make clear how or whether a strain might be identified as being BCG. Clarification is required.

With further regard to claim 55, the relationship between steps 2-3 of the claim are unclear. It is noted that step 3 refers both to contacting the probe with "the biological sample" and with "amplified sequences." It is not clear whether step 3 is to be performed using sequences amplified in step 2, or using the original "biological sample." Clarification is required.

Claim 55 remains indefinite over the recitation of the limitation "sequence of the region of sequence SEQ ID No: 2 comprising the GAG codon in positions 40 to 42 or its complementary strain" for the reasons set forth in the Office action of 1 July 2004. Specifically, first, it is unclear as to what molecules would be encompassed by the language "sequence of" a region (e.g., would this require a molecule comprising the region, subsequences of the region, etc.?). Second, there is insufficient antecedent basis for the limitation "the region of sequence...." in the claims, and further there is no clear and limiting definition in the specification as to what might constitute the "region of sequence SEQ ID No. 2 comprising the GAG codon....". Thus, it is unclear as to what "region" or portion of SEQ ID NO: 2 might be encompassed by this language. Further, it is unclear as to what "its" in claim 55 refers back to.

#### ***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

5. Claims 33, 37, and 42-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Stover et al (U.S. Patent No. 5,700,683 [12/1997; filed 2/1995]).

Stover et al disclose primers and probes that may be used to differentiate BCG strains of *M. bovis* from *M. tuberculosis* and virulent *M. bovis* strains (see entire reference, particularly column 1, line 40-column 2, line 12, and column 11, line 40-column 14, line 63). Preferred molecules disclosed by Stover et al include those of Table 1 and the primers set forth in column 14 at lines 55-62.

With regard to claim 33, it is noted that the claim merely requires a probe or primer that "hybridizes at 68°C in a 5xSSC hybridization buffer" to one of the recited molecules (which include "corresponding" RNA molecules and genes). As 5xSSC constitutes a high salt, permissive hybridization solution, the primers taught by Stover et al (all of which also meet the length requirement of the claim) anticipate the claimed invention.

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Regarding claim 37, it is further noted that several of the probes/primers of Stover et al comprises GAG and/or CTC (see, e.g., SEQ ID Nos 3-5, 9, and 11-12), and therefore meet the requirements of the claim as written.

Regarding claims 42-43, as the claim is sufficiently broad so as to encompass any primer pair "for amplification of a specific nucleotide sequence of mycobacteria of M. tuberculosis complex" in which the primers comprise any sequence of any length located outside the "senX3-regX3" region, the primer pairs of Stover et al are sufficient to meet the requirements of the claims. It is further noted that SEQ ID NO: 11 of Stover et al is 19 base pairs in length (as required by claim 43).

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).



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8. Claim 54 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stover et al (U.S. Patent No. 5,700,683 [12/1997; filed 2/1995]) in view of Ahern (The Scientist 9(15):20 [7/1995]).

Stover et al disclose primers and probes that may be used to differentiate BCG strains of *M. bovis* from *M. tuberculosis* and virulent *M. bovis* strains (see entire reference, particularly column 1, line 40-column 2, line 12, and column 11, line 40-column 14, line 63). Preferred molecules disclosed by Stover et al include the primers set forth in column 14 at lines 55-62. It is noted that the instant claim is sufficiently broad so as to encompass any primer pair "for amplification of a specific nucleotide sequence of mycobacteria of *M. tuberculosis* complex" in which the primers comprise any sequence of any length located outside the "senX3-regX3" region. Accordingly, the primer pairs of Stover et al are sufficient to meet the requirements of the claims. However, Stover et al do not teach the packaging of their primers into a kit. Ahern teaches that premade reagents provided in kit form are convenient and save researchers time and money (see p. 3/5-4/5). In view of the teachings of Ahern, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Stover et al so as to have packaged the primers taught by Stover et al into a kit. An ordinary artisan would have been motivated to have made such a modification in order to have provided the reagents needed to perform Stover et al's methods to practitioners in a convenient format for the advantages of efficiency and cost-effectiveness, as suggested by Ahern.

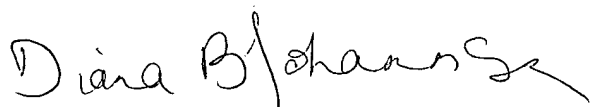
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***Conclusion***

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Diana B. Johannsen  
Primary Examiner  
Art Unit 1634